

Appl. Serial No. : 10/621,803
Response dated April 30, 2007
Reply to Office Action of Oct. 31, 2006

REMARKS

Applicant acknowledges receipt of the Office Action mailed October 31, 2006.

Claim 44 is amended herein. Claim 53 has been cancelled to better focus prosecution in the present application. New Claim 54 has been added. Support for Claim 54 can be found in the Specification in the paragraph under the heading, "Chemical Composition of Probes" (*see* particularly page 22 at lines 3-5), and in working Example 9, which describes the synthesis and use of molecular beacons comprising 2'-methoxy nucleotide analogs (*see* particularly page 47 at lines 1-2). A journal article by Majlessi et al., (Nucleic Acids Res. 26:2224-2229 (1998)) confirms that 2'-O-methyl oligonucleotide probes bound more slowly and with the same T_m to DNA targets as corresponding DNA probes (Abstract). A copy of this article is provided herewith in connection with an Information Disclosure Statement.

Claims 44-52 and 54 will be pending following entry of this Response.

Entry of this Response is respectfully requested.

The Rejections Under § 103(a)

I. The Rejection of Claims 44-52 Under § 103(a)

Claims 44-52 have been rejected under 35 U.S.C. § 103(a) over the combined disclosure contained in U.S. Patent No. 6,060,288 ("**Adams**" hereafter), *Nature Biotechnol.*, **17**:804-807 (1999) ("**Whitcombe**" hereafter), and *Histochem. Cell Biol.* **108**:431-437 (1997) ("**Mueller**" hereafter). According to the rejection, **Adams** instructs a solid support bead comprising a surface-immobilized

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amplification primer, but fails to instruct either immobilized labeled probes or amplification using primers comprising a promoter for an RNA polymerase. **Whitcombe** is cited for teaching amplification of target nucleic acids using "Scorpion" primers which include both probe and primer elements. **Mueller** is cited for teaching amplification of RNA targets using the "3SR" sequence replication method which uses a primer containing a T7 promoter sequence. According to the rejection, an ordinary skilled artisan would have been motivated to use the Scorpion primer of **Whitcombe** as one of the primers in the amplification device of **Adams** because **Whitcombe** instructs numerous advantages of unimolecular (*i.e.*, resulting from an integral probe/amplicon structure) binding events used in the detection procedure. Further according to the rejection, it would have been obvious for an ordinary skilled artisan to have used the 3SR reagents of **Mueller** in the device of **Adams** and **Whitcombe** because **Mueller** instructs that the 3SR technique is simple to perform, there is no need for a thermal cycler or for heat stable enzymes, there is no need for denaturing conditions, etc.

The invention defined by the amended claims cannot be considered *prima facie* obvious because all of the claim limitations are not suggested by the prior art. Independent Claim 44 has been amended to specify that the labeled hybridization probe immobilized to the surface of the solid support is "separate from the amplification primer." Applicant relies on the ordinary meaning of "separate" as, "not joined." The amendment is supported generally by the Specification which discusses independent synthesis and immobilization procedures for probes and primers of the invention. For example, in a description of an exemplary composite array prepared on the inner bottom surface of a plastic multiwell plate, the Specification on page 13 at lines 5-7 recites,

"The composite array is prepared by first arraying the probes, and then contacting the entire bottom surface of the well, including the arrayed portion, with a solution containing the amplification primer."

Clearly, the probes and primers are separate molecules (*i.e.*, not joined together) because they were

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capable of immobilization at different times. The Specification on page 14 at lines 16-20 recites,

“Sites on the solid support surface of the composite array that are not occupied by bonds to the immobilized hybridization probes desirably are occupied by bonds to oligonucleotide primers, thereby resulting in a substantially uniform distribution of primers over the surface of the composite array.”

Again, the probes and primers must have been separate from each other, as they were capable of independent immobilization to the solid support surface. Finally, the fact that probes and primers of the invention are separate was acknowledged in the prosecution history of the instant Application. Indeed, the Office Action mailed November 14, 2005 stated (*see* bottom of page 4),

“First, there are lots of areas which are excluded from occupation by the primers, the most obvious are the areas in which the probes are bound, since the oligonucleotides physically cannot be bound in the same spots as the probes.”

If the probes and primers of the invention physically cannot bind in the same spots as the probes, then it reasonably follows that they are “separate from” each other. Nothing in any of the cited references provide any suggestion that would lead one of ordinary skill in the art to employ a labeled hybridization probe immobilized to the solid support surface separate from the amplification primer.

Since independent Claim 44 has been amended to require a labeled hybridization probe separate from the amplification primer, and since the prior art does not teach or suggest this limitation in the context of the claimed combination, the invention of Claim 44 cannot be considered obvious in light of the prior art. Once an independent claim is found nonobvious under 35 U.S.C. § 103, any claim depending therefrom is also nonobvious (see MPEP § 2143.03). Accordingly, Claims 45-52 also are nonobvious, and so withdrawal of the § 103 rejection is appropriate.

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II. The Rejection of Claim 53 Under § 103(a)

Claim 53 has been rejected under 35 U.S.C. § 103(a) over the combined disclosure **Adams, Whitcombe and Mueller**, further in view of U.S. Patent No. 6,310,354 ("**Hanninen**"). The rejection of Claim 53 is no longer relevant in view of the cancellation of that claim.

CONCLUSION

In view of the above, it is submitted that the claims are in condition for allowance. Reconsideration and withdrawal of all outstanding rejections are respectfully requested. Allowance of the claims at an early date is solicited. If any points remain that can be resolved by telephone, the Examiner is invited to contact the undersigned at the telephone number shown below.

DEPOSIT ACCOUNT INFORMATION

Please charge any fees due in connection with this Reply, including the fee for a three-month extension of time, to Deposit Account No. 07-0835 in the name of Gen-Probe Incorporated.

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CERTIFICATE OF MAILING

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is being deposited on the date indicated below with the U.S. Postal Service as first class mail addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Respectfully submitted,

GEN-PROBE INCORPORATED

Dated: April 30, 2007

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